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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,074	02/15/2002	Matthew C. Coffey	032775-091	8498
26181	7590	10/18/2006	EXAMINER	
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			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/076,074

Applicant(s)

COFFEY ET AL.

Examiner

Bao Qun Li

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,8-11,16,22 and 26-59 is/are pending in the application.
- 4a) Of the above claim(s) 31-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6,8-11,16,27-30 and 35-59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Response to Amendment

This is a response to the amendment filed on 08/09/06. Claims 1-5, 7, 12-15, 17-21, 23-25 were canceled. Claims 26, 27, 28 have been amended. New claims 51-59 have been added. Claims 31-34 were withdrawn from the consideration, Claims 6, 8-11, 16, 22, 26-59 are pending. Claims 6, 8-11, 16, 22, 26-30 and 35-59 are considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
2. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
3. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).
4. Claims 6, 8-11, 16, 22, 26-29, 35-42, 44-50, 52-59 are still rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 28 of U.S. Patent No. 6,565,831B1) or claims 1, 2-8, 13-20, 24-34 of Lee et al. (US Patent No. 6,136,307A) in view of disclosure of Smith (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

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5. Applicants traverse the rejection and submit that none of these documents even teach or suggest a drug resistance to a chemotherapeutic agent, nor how one would select a subject for treatment who has a neoplasm capable of developing drug resistance. In particular, applicants argue that the '831 patent or '307 patent, either alone or in combination with the Smith reference do not teach or suggest to prevent a ras-activated neoplasm from developing drug resistance to a chemotherapeutic agent y using the reovirus in combination with reovirus.

6. Applicants' argument has been respectfully considered; however, it is not found persuasive. Because as applicants submit that the phrase "(a) identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent or refractory to a chemotherapeutic agent occurs inherently during the treatment of a subject who comprises neoplastic cells susceptible to a chemotherapeutic agent or refractory to a chemotherapeutic agent."

7. Regarding the limitation of preventing a ras-activated neoplasm from development of a drug resistance to a chemotherapeutic agent is not considered as an active step, because it merely cites the purpose of the method and it does not add any manipulation step of the claimed method. To this context, there is not more step different from the disclosure by cited patent "831" or 307". Moreover, applicants submit in the response that the identification process could inherently exist during the treatment via co-administering the reovirus and chemotherapeutic agent together. To this context, there is not extra step or different step from the method cited patent "307" or "051A2".

8. Hence, the rejected claims would have been obvious over the reference claim(s). In fact, Smith's reference only serves to support the motivation why an ordinary skilled in the art like to combine an oncolytic virus therapy with a chemotherapy because Smith et al clear teach that the combination therapy of an oncolytic virus with a chemotherapeutic agent produces a synergistic effect. An ordinary skilled in the art would obviously select to use such combinatory therapy to produce the more significant anti-tumor effect then use any of them alone.

9. The rejections over both patents are therefore, maintained.

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10. Claims 27, 35-42, 52, 53, 54, 55, 56, 57 are still rejected under 35 U.S.C. 102(a) as being anticipated by Lee et al. (A) (US Patent No. 6,136,307A) or Lee et al. (B) (WO 00/50051A2).

11. Applicants traverse the rejection and submit that neither the '307 patent nor the '051 application teach all the limitations of the independent claims, such as: a step of "identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" as required by claim 26; a step of "administering, to a subject having a ras-activated neoplasm capable of developing drug resistance to a chemotherapeutic agent, an effective amount of reovirus" as required by claim 27; or a step of "determining, in a subject having a ras-activated neoplasm, if the ras activated neoplasm includes ras-activated neoplastic cells that are refractory to a chemotherapeutic agent" as required by claim 28. Moreover, applicants argue that neither the '307 patent nor the '051 application teach the development of resistance to a chemotherapeutic agent, let alone the specific limitations of the instant claims.

12. Applicants' argument has been respectfully considered; however, it is not found persuasive. Because in claims 27, 53 and 57 drafted, the administration of reovirus take places currently or prior to the administration of the chemotherapeutic agent. The identification step therefore, occur concurrently with the steps (b) and (c). Moreover, applicants submit that the identification process could inherently exist during the treatment via co-administering the reovirus and chemotherapeutic agent together. To this context, there is not extra step or different step from the method cited patent "307" or "051A2".

13. Regarding the limitations of "preventing", it is still not considered as an active step in the claimed invention, because it does not add any active step of the claimed method.

14. The rejection is still maintained.

Claim Rejections - 35 USC § 103

15. Claims 6, 8-11, 16, 22, 26-29, 35-42, 44-50, 52-59 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US Patent No. 6,136,307A) or Lee et al. (B) (WO 00/50051A2) or over Mercer University (Mercer University Home page 1996, pp. 1-2) in view of Smith (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

16. Applicants traverse the rejections and submit that none of the cited reference teach or suggest the limitations of the independent claims 26, 27, and 28, such as: a step of "identifying a

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subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" as required by claim 26; a step of "administering, to a subject having a ras-activated neoplasm capable of developing drug resistance to a chemotherapeutic agent, an effective amount of reovirus" as required by claim 27; or a step of "determining, in a subject having a ras-activated neoplasm, if the ras activated neoplasm includes ras-activated neoplastic cells that are refractory to a chemotherapeutic agent" as required by claim 28. Moreover, applicants argue that none of these documents even teach or suggest drug resistance of a ras-activated neoplasm to a chemotherapeutic agent, nor how one would select a subject for treatment that has a ras-activated neoplasm capable of developing drug resistance. Smith's reference does not remedy the defect.

17. Applicants' argument has been respectfully considered. However, it is not found persuasive because

18. In the instant case, in the response filed on Feb. 23, 2006, applicants interpret that the identification step of (a) in claims 26, 27 and 28 occur concurrently with the steps (b) and (c) of administering the reovirus and chemotherapeutic agent. To this context, the following rejection is still applied. Moreover, the limitation of preventing a ras-activated neoplasm from developing drug resistance to a chemotherapeutic agent is not considered as an active step in all claims because it merely cites the purpose of the method and it does not add any manipulation step of the claimed method.

19. Therefore, it would have been obvious for a person with ordinary skill in the art to be motivated using less dosage of therapeutic agent in combination of the oncolytic reovirus to treat ras-mediated neoplasm with much better anti-tumor effect since reovirus is particularly suitable for oncolyzing the ras-mediated neoplastic cell and combination of reovirus with a chemotherapeutic agent produces a synergistic effect. The claimed invention is *prima facie* obvious absent unexpected results.

New ground rejection:

Claim Rejections - 35 USC § 112

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 30, 43, and 51 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having a method for using reovirus treatment to restore a drug sensitivity of a ras mediated neoplasm to a previous resistant chemotherapeutic agent, does not reasonably provide enablement for having a method for using reovirus treatment to prevent a ras-mediated neoplasm from developing drug resistant to a second chemotherapeutic agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

22. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See *United States v. Theketrone Inc.*, 8USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following: 1). The nature of the invention, 2). The state of art, 3). Unpredictability of the field, 4). Number of working examples, 5). Amount of guidance presented in the specification, 6). Scope of the invention; and 7). Level of the skill in the art.

23. The nature of the invention is directed to use reovirus treatment to restore the chemotherapeutic sensitivity to a ras-mediated neoplasm to a previous resistant chemotherapeutic agent. However, the scope of the invention is directed to using the reovirus to prevent any drug resistance to any second chemotherapeutic agent for a ras-mediated neoplasm. The state of art teaches that cancer cell has an ability to gain a drug resistant to any chemotherapeutic agent. However, whether a neoplasm gains such resistance is random and largely unknown. Therefore, it is unpredictable whether a ras-mediated neoplasm is resistant to a chemotherapeutic agent in advance. The specification only teaches that a reovirus treatment to a neoplasm that is refractory to cisplatin treatment unexpectedly restore the chemotherapeutic sensitivity of said neoplasm to the resistant cisplatin. However, the specification does not teach

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such treatment can prevent the neoplasm from developing a drug resistance to another unknown chemotherapeutic agent. As described above, whether a neoplasm will develop a drug resistance is largely unknown. The specification does not teach or give guidance about how to predict or measure whether the reovirus treatment can be used for preventing a drug resistance to an unknown second chemotherapeutic agent.

Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BAOQ...
PATENT EXAMINER

Bao Qun Li

05/09/06

